

CLAIMS

1. A crystalline or crystal-like lipopeptide or a salt thereof, wherein the lipopeptide is selected from the group consisting of daptomycin, A54145 and a daptomycin-related lipopeptide.
2. The crystalline or crystal-like lipopeptide or salt thereof, according to claim 1, wherein the salt is a divalent calcium salt.
3. The crystalline or crystal-like lipopeptide antibiotic or salt thereof, according to claim 1, wherein the lipopeptide antibiotic is daptomycin.
4. The crystalline or crystal-like lipopeptide or salt thereof, according to claim 3, wherein the salt is a divalent calcium salt.
5. The crystalline daptomycin according to claim 3, wherein an x-ray diffraction pattern of the crystalline daptomycin, using a Cu ($\lambda=1.54 \text{ \AA}$) x-ray source, has a diffraction angle (2θ) = 10.9, 19.2 and 23.3 (degree) or a diffraction angle (2θ) = 19.2, 23.2, 23.4 and 23.6 (degree).
6. The crystal-like lipopeptide according to claims 1-4, wherein crystal-like means the compound has crystalline characteristics by birefringence, but does not have crystalline characteristics by x-ray powder diffraction.
7. The crystalline or crystal-like daptomycin according to claim 3, wherein the crystalline or crystal-like daptomycin comprises urchin-like or a cluster of needles, needle-like, or rod-like crystals.
8. The crystalline or crystal-like daptomycin according to claim 3, wherein the crystalline daptomycin has a purity of at least 95%.

9. The crystalline or crystal-like daptomycin according to claim 3, wherein the crystalline daptomycin or salt thereof has a purity of at least 97%.

10. The crystalline or crystal-like daptomycin according to claim 3, wherein the crystalline daptomycin or salt thereof contains no single impurity greater than 1%.

11. The crystalline or crystal-like daptomycin according to any one of claims 8-10, wherein the purity is measured by HPLC.

12. The crystalline or crystal-like lipopeptide according to claim 1, wherein a crystal of the lipopeptide is at least 5 μm .

13. The crystalline or crystal-like lipopeptide according to claim 12, wherein the crystal is at least 50 μm .

14. The crystalline or crystal-like lipopeptide according to either of claims 12 or 13, wherein the lipopeptide is daptomycin.

15. The crystalline lipopeptide according to claim 1, wherein the crystalline lipopeptide exhibits a higher stability than an amorphous form of the lipopeptide.

16. The crystalline lipopeptide according to claim 15, wherein the crystalline lipopeptide exhibits higher stability to heat, light, degradation or humidity than the amorphous form.

17. The crystalline lipopeptide according to claim 16, wherein the stability is measured by antibiotic activity or degradation of the lipopeptide antibiotic.

18. The crystalline lipopeptide according to claim 15, wherein the lipopeptide is daptomycin.

19. The crystalline daptomycin according to claim 18, wherein the crystalline lipopeptide exhibits lower conversion to anhydro-daptomycin or the β -isomer of daptomycin than the amorphous form of daptomycin.

20. The crystalline lipopeptide according to claim 1, which is a daptomycin-related lipopeptide.

21. A pharmaceutical composition comprising a crystalline or crystal-like lipopeptide antibiotic and a pharmaceutically acceptable carrier, wherein the lipopeptide antibiotic is selected from the group consisting of daptomycin, A54145, and a daptomycin-related lipopeptide.

22. The pharmaceutical composition according to claim 21, wherein the crystalline or crystal-like lipopeptide is daptomycin.

23. The pharmaceutical composition according to claim 22, wherein the crystalline or crystal-like daptomycin is enterically coated for oral administration.

24. The pharmaceutical composition according to claim 22, wherein the crystalline or crystal-like daptomycin is formulated in a dose of 3 to 75 mg/kg.

25. The pharmaceutical composition according to claim 22, wherein the carrier enhances the oral availability of daptomycin.

26. The pharmaceutical composition according to claim 22, which is in the form of micronized particles or microspheres.

27. A container comprising the pharmaceutical composition according to claim 21.

28. The pharmaceutical composition according to claim 26, which is used as an aerosol.

29. A formulation comprising a crystalline or crystal-like lipopeptide antibiotic and a pharmaceutically acceptable carrier, wherein the lipopeptide antibiotic is selected from the group consisting of daptomycin, A54145 and a daptomycin-related lipopeptide.

30. The formulation according to claim 29, which is a pharmaceutical formulation, a food formulation, a feed formulation, a veterinary formulation, a cosmetic formulation or a personal care formulation.

31. The formulation according to claim 29, that is a pharmaceutical formulation, wherein the formulation further comprises another antibiotic, a stabilizing agent, an agent to aid in absorption, a pH buffering agent or an inorganic salt.

32. The formulation according to claim 29 that is a feed formulation, wherein the formulation further comprises animal feed and may optionally comprise another antibiotic or vitamins.

33. The formulation according to claim 29, that is a personal care formulation, wherein the personal care formulation is a washing formulation, a soap, a shampoo or an antiperspirant.

34. The formulation according to claim 29, that is a veterinary formulation, wherein the formulation is a soap, a shampoo or a pharmaceutical composition.

35. A method for administering a crystalline or crystal-like lipopeptide, a pharmaceutically acceptable salt thereof or a pharmaceutical composition thereof, wherein the lipopeptide is selected from the group consisting of daptomycin, A54145 and a daptomycin-related lipopeptide, comprising the step of administering to a patient in need thereof a therapeutically effective amount of the crystalline or crystal-like lipopeptide, the pharmaceutically acceptable salt thereof or the pharmaceutical composition thereof.

36. The method according to claim 35, wherein the lipopeptide antibiotic has a purity of greater than 95%.

37. The method according to claim 36, wherein the lipopeptide antibiotic is daptomycin.

38. The method according to claim 37, wherein the daptomycin is a crystalline daptomycin and an x-ray diffraction pattern of the crystalline daptomycin has a diffraction angle (2θ) = 10.9, 19.2 and 23.3 (degree) using a Cu ($\lambda=1.54 \text{ \AA}$) x-ray source.

39. The method according to claim 37, wherein the daptomycin is a crystal-like daptomycin and the crystal-like daptomycin has crystalline characteristics by birefringence but does not have crystalline characteristics by x-ray powder diffraction.

40. The method according to claim 35, wherein the crystalline or crystal-like lipopeptide is administered as a micronized particle.

41. The method according to claim 35, wherein the crystalline or crystal-like lipopeptide is administered as a targeted release form.

42. The method according to either of claims 40 or 41, wherein the lipopeptide is daptomycin.

43. The method according to claim 35, wherein the oral administration is done subcutaneously, intravenously or intramuscularly.

44. A method for storing a lipopeptide, wherein the lipopeptide is selected from the group consisting of daptomycin, A54145 and a daptomycin-related lipopeptide, comprising the steps of

- a) providing a dissolved solution of a lipopeptide;
- b) crystallizing or precipitating the lipopeptide;
- c) collecting and drying the lipopeptide; and
- d) storing the lipopeptide;

wherein the crystalline or crystal-like lipopeptide is more stable than an amorphous form of the lipopeptide.

45. A method for manufacturing a crystalline or crystal-like lipopeptide, wherein the lipopeptide is selected from the group consisting of daptomycin, A54145 and a daptomycin-related lipopeptide, comprising the steps of

- a) providing an amorphous form of a lipopeptide;
- b) crystallizing or precipitating the lipopeptide; and
- c) collecting the crystalline or crystal-like lipopeptide.

46. The method according to claim 44, wherein said collecting is performed by filtration.

47. The method according to claim 46, further comprising the step of washing the lipopeptide after step b).

48. The method according to either of claims 45 or 46, further comprising the step of drying the lipopeptide after step c).

49. The method according to claim 48, further comprising the step of sterilizing the lipopeptide after drying.

5 50. The method according to claim 45, wherein step c) is performed under sterile conditions.

51. The method according to claim 50, wherein step b) is performed under sterile conditions.

10 52. The method according to claim 51, further comprising the step of drying the lipopeptide after step c) under sterile conditions.

15 53. The method according to claim 44, wherein the purity of the crystalline lipopeptide is higher than the amorphous form of the lipopeptide.

54. The method according to claim 53, wherein the purity of the amorphous form is approximately 90% and the purity of the crystalline or crystal-like form is greater than 95%.

20 55. The method according to claim 53, wherein the purity of the amorphous form is approximately 93%, and the purity of the crystalline or crystal-like form is greater than 95%.

25 56. The method according to claim 53, wherein the purity of the amorphous form is approximately 93%, and the purity of the crystalline or crystal-like form is approximately 98%.